

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Bunick, et al.	Confirmation No.:	9623
Appln. No.	:	09/752,899	Examiner:	L.S.Channavajjala
Filed	:	December 29, 2000	Group Art Unit:	1615
Filing Date	:	09/28/2002		
Title	:	SOFT TABLET CONTAINING DEXTROSE MONOHYDRATE		

DECLARATION UNDER 37 CFR 1.132

I have reviewed the office action and have given consideration to the combination of dextrose monohydrate and a high intensity sweetener. I believe that it is non-obvious to combine dextrose monohydrate, as referenced in US 4,684,534 (Valentine), with sucralose, as referenced in US 6,667,050 (Boissonneault). Dextrose monohydrate is a preferred material in a chewable dosage form due to its superior mouthfeel over dextrose. However, the addition of a high intensity sweetener (such as aspartame) to dextrose monohydrate in a dosage form that contains a pharmaceutical active is disadvantageous for several reasons. Aspartame is an amine based compound that will react with dextrose over time, resulting in discoloration and browning of a tablet. This reaction can be exacerbated by the presence of water in a chewable tablet.

Dextrose monohydrate contains a high level of bound water, which can be released more readily upon storage in high temperature environments. Various temperatures are required for testing of products containing pharmaceutical active ingredients, including temperatures of 40 and 50 degrees Celsius. It is also not uncommon for temperatures of up to 70 degrees Celsius to be experienced upon transport or storage of pharmaceutical products. Dextrose monohydrate has a relatively high water liability and as temperatures increase, a release of the bound water can occur, resulting in a subsequent reaction within the tablet between dextrose and excipients (i.e. inactive ingredients) or active ingredients. This is shown in the attached Material Safety Data Sheet from Mallickrodt Baker, Inc. for dextrose monohydrate. In US Patent 6,814,978 the application of heat energy to release the bound water of a hydrate is highlighted as a

means for softening a tablet prior to packaging, in compositions where the tablet comprises dextrose monohydrate.

Furthermore, water that is released from a hydrate is more readily available to promote these interactions in a closed packaging system such as a blister or a bottle since it is not released to the outer environment. As outlined in the present invention, it has been found that sucralose is a high intensity sweetener that does not react with dextrose in the presence of increased levels of water.

I, Frank J. Bunick, hereby declare:

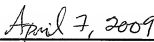
1. I am one of the joint inventors of the U.S. Patent Application Serial No. 10/476,504, entitled "MODIFIED RELEASE DOSAGE FORMS" identified above.

2. I have been employed by McNEIL-PPC, Inc. since April 29th 1996, in the positions of Senior Research Scientist (1996-1997), Principal Scientist (1997-1999), Research Fellow (1999-2005), and Director 2005- Present My technical experience includes, but is not limited to, development of novel solid and liquid dosage form technologies and evaluation of new product & process technologies.

3. I received a Ph.D. degree in Food Science & Nutrition in 1985 from the University of Massachusetts, a Master of Science degree in Health Science from Northeastern University in 1979, and a Bachelor of Arts & Science degree in Chemistry & Biology from the University of Massachusetts in 1973.



Frank Bunick



Date:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18

U.S.C. 1001 and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

MSDS Number: **D0832** \* \* \* \* \* Effective Date: 11/21/08 \* \* \* \* \* Supersedes:  
01/19/06

**MSDS**

**Material Safety Data Sheet**

From: Mallinckrodt Baker, Inc.  
222 Red School Lane  
Phillipsburg, NJ 08865



Mallinckrodt  
CHEMICALS



24 Hour Emergency Telephone: 800-455-2151  
CHEMTREC: 1-800-424-9300

National Response In Canada  
CANUTEC: 613-996-6666

Outside U.S. and Canada  
Chemtree: 703-527-3867

NOTE: CHEMTREC, CANUTEC and National Response Center emergency numbers to be used only in the event of chemical emergencies involving a spill, leak, fire, exposure or accident involving chemicals.

All non-emergency questions should be directed to Customer Service (1-800-582-2537) for assistance.

# DEXTROSE MONOHYDRATE POWDER USP

## 1. Product Identification

**Synonyms:** D-glucose, monohydrate; dextrosol; dextrose, monohydrate, powder

**CAS No.:** 50-99-7 (Anhydrous) 5996-10-1 (Monohydrate)

**Molecular Weight:** 198.18

**Chemical Formula:** C<sub>6</sub>H<sub>12</sub>O<sub>6</sub>.H<sub>2</sub>O

**Product Codes:**

J.T. Baker: 1910, 1912, 1913

Mallinckrodt: 8834

## 2. Composition/Information on Ingredients

Ingredient	CAS No	Percent	Hazardous
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### 3. Hazards Identification

#### Emergency Overview

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**As part of good industrial and personal hygiene and safety procedure, avoid all unnecessary exposure to the chemical substance and ensure prompt removal from skin, eyes and clothing.**

**SAF-T-DATA<sup>(tm)</sup> Ratings** (Provided here for your convenience)

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Health Rating: 0 - None

Flammability Rating: 1 - Slight

Reactivity Rating: 1 - Slight

Contact Rating: 0 - None

Lab Protective Equip: GOGGLES; LAB COAT; PROPER GLOVES

Storage Color Code: Green (General Storage)

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#### Potential Health Effects

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**Inhalation:**

Not expected to be a health hazard.

**Ingestion:**

Extremely large oral dosages may produce gastrointestinal disturbances.

**Skin Contact:**

No adverse effects expected.

**Eye Contact:**

No adverse effects expected but dust may cause mechanical irritation.

**Chronic Exposure:**

No information found.

**Aggravation of Pre-existing Conditions:**

No information found.

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## 4. First Aid Measures

**Inhalation:**

Not expected to require first aid measures.

**Ingestion:**

Not expected to require first aid measures.

**Skin Contact:**

Not expected to require first aid measures.

**Eye Contact:**

Wash thoroughly with running water. Get medical advice if irritation develops.

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## 5. Fire Fighting Measures

**Fire:**

Not considered to be a fire hazard.

**Explosion:**

Not considered to be an explosion hazard.

**Fire Extinguishing Media:**

Use any means suitable for extinguishing surrounding fire.

**Special Information:**

Use protective clothing and breathing equipment appropriate for the surrounding fire.

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## 6. Accidental Release Measures

Ventilate area of leak or spill. Wear appropriate personal protective equipment as specified in Section 8. Spills: Sweep up and containerize for reclamation or disposal. Vacuuming or wet sweeping may be used to avoid dust dispersal.

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## 7. Handling and Storage

Keep in a tightly closed container, stored in a cool, dry, ventilated area. Protect against physical damage. Isolate from incompatible substances. Containers of this material may be hazardous when empty since they retain product residues (dust, solids); observe all warnings and precautions listed for the product.

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## 8. Exposure Controls/Personal Protection

### **Airborne Exposure Limits:**

None established.

### **Ventilation System:**

In general, dilution ventilation is a satisfactory health hazard control for this substance. However, if conditions of use create discomfort to the worker, a local exhaust system should be considered.

### **Personal Respirators (NIOSH Approved):**

For conditions of use where exposure to dust or mist is apparent and engineering controls are not feasible, a particulate respirator (NIOSH type N95 or better filters) may be worn. If oil particles (e.g. lubricants, cutting fluids, glycerin, etc.) are present, use a NIOSH type R or P filter. For emergencies or instances where the exposure levels are not known, use a full-face positive-pressure, air-supplied respirator. **WARNING:** Air-purifying respirators do not protect workers in oxygen-deficient atmospheres.

### **Skin Protection:**

Wear protective gloves and clean body-covering clothing.

### **Eye Protection:**

Use chemical safety goggles. Maintain eye wash fountain and quick-drench facilities in work area.

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## 9. Physical and Chemical Properties

### **Appearance:**

Colorless crystals or white crystalline powder.

### **Odor:**

Odorless.

### **Solubility:**

ca. 1 g/1.1 ml water @ 25C (77F).

### **Specific Gravity:**

1.54

### **pH:**

5.9 For 0.5 M aqueous solution  
% Volatiles by volume @ 21C (70F):

0

**Boiling Point:**

No information found.

**Melting Point:**

83C (181F)

**Vapor Density (Air=1):**

No information found.

**Vapor Pressure (mm Hg):**

No information found.

**Evaporation Rate (BuAc=1):**

No information found.

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## 10. Stability and Reactivity

**Stability:**

Stable under ordinary conditions of use and storage. < 50C the Hydrated crystalline form is stable.

**Hazardous Decomposition Products:**

Carbon dioxide and carbon monoxide may form when heated to decomposition.

**Hazardous Polymerization:**

Will not occur.

**Incompatibilities:**

Reacts with sodium nitrite plus potassium nitrite, sodium peroxide plus potassium nitrate.

**Conditions to Avoid:**

Heat, incompatibles.

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## 11. Toxicological Information

Investigated as a tumorigen, mutagen, reproductive effector. For Dextrose (anhydrous): Oral rat LD50: 25800 mg/kg .

-----\Cancer Lists\-----

---NTP Carcinogen---

Ingredient

Known Anticipated IARC Category

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Dextrose Anhydrous (50-99-7)

No

No

None

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## 12. Ecological Information

### **Environmental Fate:**

No information found.

### **Environmental Toxicity:**

No information found.

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## 13. Disposal Considerations

Whatever cannot be saved for recovery or recycling should be managed in an appropriate and approved waste disposal facility. Processing, use or contamination of this product may change the waste management options. State and local disposal regulations may differ from federal disposal regulations. Dispose of container and unused contents in accordance with federal, state and local requirements.

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## 14. Transport Information

Not regulated.

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## 15. Regulatory Information

-----\Chemical Inventory Status - Part 1\-----

Ingredient

TSCA EC Japan Australia

Dextrose Anhydrous (50-99-7)

Yes Yes Yes Yes

-----\Chemical Inventory Status - Part 2\-----

--Canada--

Ingredient	Korea DSL	NDSL	Phil.
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Dextrose Anhydrous (50-99-7)	Yes	Yes	No Yes

-----Federal, State & International Regulations - Part 1)-----

-SARA 302- -----SARA 313-----

Ingredient	RQ	TPQ	List	Chemical Catg.
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Dextrose Anhydrous (50-99-7)	No	No	No	No

-----Federal, State & International Regulations - Part 2)-----

-RCRA- -TSCA-

Ingredient	CERCLA	261.33	8(d)
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Dextrose Anhydrous (50-99-7)	No	No	No

Chemical Weapons Convention: No TSCA 12(b): No CDTA: No

SARA 311/312: Acute: No Chronic: No Fire: No Pressure: No

Reactivity: No (Pure / Solid)

**Australian Hazchem Code:** None allocated.

**Poison Schedule:** None allocated.

**WHMIS:**

This MSDS has been prepared according to the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

## 16. Other Information

**NFPA Ratings:** Health: 0 Flammability: 0 Reactivity: 0

**Label Hazard Warning:**

As part of good industrial and personal hygiene and safety procedure, avoid all unnecessary exposure to the chemical substance and ensure prompt removal from skin, eyes and clothing.

**Label Precautions:**

None.

**Label First Aid:**

Not applicable.

**Product Use:**

Laboratory Reagent.

**Revision Information:**

No Changes.

**Disclaimer:**

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**Prepared by:** Environmental Health & Safety

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